REMARKS

Claims 2-6 and 74-78 are pending in this application. Claims 3 and 75 are amended to recite a stereomerically pure isomer when R_1 and R_2 are both methyl. Support for this amendment can be found, for example, on page 13, lines 1-2; page 13, lines 20-21 to page 14, lines 1-3; and page 15, lines 10-14 to page 16, lines 1-5. No new matter has been introduced.

Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

I. The Rejection under 35 U.S.C. §103 Should be Withdrawn.

Claims 2-6 and 74-78 are rejected under 35 U.S.C. 103(a) as allegedly obvious over the combined teachings of Jeffery *et al.*, *J. Chem. Soc. Perkin Trans.*, 1: 2583-9 (1996) ("Jeffery") and Housley *et al.*, US Patent No. 5,047, 432 ("Housley"). (Office Action, page 2). Applicants respectfully traverse this rejection.

The U.S. Supreme Court has recently addressed the test for obviousness under 35 U.S.C. § 103.[1] (*KSR International Co. v. Teleflex Inc.* 127 S.Ct. 1727, 167 L.Ed.2d 705, 75 USLW 4289, 82 U.S.P.Q.2d 1385 (2007)). In *KSR*, the Supreme Court rejected the Federal Circuit's *rigid* application of the "teaching, suggestion, motivation" test ("the TSM test") in determining obviousness in the particular case in question. (*Id.* at 1739). According to the Supreme Court, the correct standard to apply is set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966). (*Id* at 1734). The Graham factual inquires, which establish a guide for determining obviousness, are: (1) determining the scope and contents of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the pertinent art; and (4) evaluating any evidence of secondary considerations. (*KSR,* 127 S.Ct. at 1734 (*citing Graham*, 383 U.S. at 15-17)).

However, the *KSR* decision indicated that while the TSM test is not the sole method for determining obviousness, it may still be a factor. (*Id.* at 1741). Indeed, following the *KSR* decision, the Federal Circuit noted the helpfulness of the TSM test in chemical cases. (*Takeda Chemical Industries, Ltd. v. Alphapharm Pty.*, Ltd. 492 F.3d 1350 (C.A.Fed. (N.Y.)), 83 U.S.P.Q.2d 1169 (2007)). Specifically, the Federal Circuit noted that "there is

[1] "The Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness." (Manual of Patent Examining Procedure ("MPEP"), §2142).

'no necessary inconsistency between the idea underlying the TSM test and the Graham analysis.'...[a]s long as the test is not applied as a 'rigid and mandatory' formula." (*Id.* at 1357, *quoting KSR*, 127 S.Ct. at 1731). The Court concluded:

> in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.

(*Id.*, emphasis added).

Turning to the instant case, based on the principles set forth by the decisions in *KSR* and *Takeda*, Applicants respectfully submit that 1) the Examiner has not established a *prima facie* case of obviousness, and 2) even if, *arguendo*, a *prima facie* case of obviousness were established, such a *prima facie* case is rebutted because Jeffery teaches away from the claimed invention.

1. The Examiner has not established a prima facie case of obviousness.

The Examiner alleges that the pending claims are obvious based on the assertion that "Jeffery *et al.* teaches stereoisomers of hydroxylated derivative of sibutramine, similar to claimed herein" and "Housley is teaching that structurally similar compounds as claimed inherein [sic] can exist in different optically active form." (Office Action, page 2). Applicants respectfully disagree.

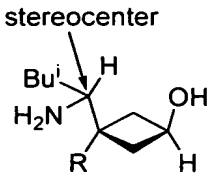
First, while the Examiner has relied upon allegations of structural similarity, Applicants respectfully remind the Examiner that such reliance is legally improper in establishing a *prima facie* case of obviousness.[2] This is because, as is known to one of skill in the art, even slight modifications in structure can have substantial effects on the properties of a compound. Indeed, Courts have repeatedly refused to find obviousness on the basis of mere allegations of structural similarity. (*See e.g.* MPEP § 2144.08, citing James Darnell *et al.*, Molecular Cell Biology 51 (2 ed. 1990) ("the gain or loss of even one methyl group can

[2] The Examiner has alleged that "Jeffery et al. teaches stereoisomers of hydroxylated derivative of sibutramine, similar to claimed herein." (Office Action, page 2) (emphasis added). Further, the Examiner has alleged that "Housley et al. is teaching that structurally similar compounds as claimed inherein [sic] can exist in different optically active form..." (Office Action page 2) (emphasis added). In addition, the Examiner has alleged that "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify Jeffrey et al., by including diastereoimers and multiple chiral centers in the compounds as taught by Housley et al., because the latter reference is expressly teaching that diastereomers and multiple chiral centers are old in the structurally similar compounds." (Office Action, pages 2-3) (emphasis added).

destabilize the structure [of proteins]..."); MPEP § 2144.09, citing *In re Langer*, 465 F.2d 896, 175 U.S.P.Q. 169 (CCPA 1972) (claims to a polymerization process using an amine were held unobvious over a similar prior art process because of steric differences even though claimed amine differed by only 3 carbon atoms); MPEP § 2144.09, citing *Ex parte Blattner*, 2 U.S.P.Q.2d 2047 (Bd. Pat. App. & Inter 1987) (claims directed to compounds containing a 7-membered ring held unobvious over a reference which taught 5- and 6- membered ring homologs of the claimed compounds) MPEP § 2144.09, citing *In re Mills*, 281 F.2d 218, 126 U.S.P.Q. 513 (C.C.P.A. 1960) (claims to C1 alkyl sulfate held to be unobvious over prior art disclosure of C8 to C12 alkyl sulfates); MPEP § 2144.09, citing *Ex parte Mowry*, 91 U.S.P.Q. 219 (Bd. App. 1950) (claimed cyclohexylstyrene held not to be *prima facie* obvious over prior art isohexylstyrene); MPEP § 2144.09, citing *In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992) (obviousness rejection of novel dicamba salt with acyclic structure reversed even though prior art reference taught broad prior genus encompassing claimed salt because disclosed examples of genus were dissimilar in structure, lacking an ether linkage or being cyclic)). Therefore, the mere disclosure of "structurally similar" compounds by the Jeffery and/or Housley references cannot render the claimed compounds obvious.

Second, while the Examiner points to several specific compounds in Jeffery and alleges that such compounds are stereomerically pure,[3] none of the compounds pointed to by the Examiner are described by Jeffery as stereomerically pure, contrary to the Examiner's allegation. Specifically, with regard to compound 5a, Applicants respectfully point out that Jeffery merely indicates cis/trans isomerism with respect to the substituents on the cyclobutyl ring. However, as shown below, Jeffery is completely silent with regard to the stereoconfiguration (*e.g.* R or S) of the carbon bearing the isobutyl moiety. Further, lacking is any teaching or suggestion of the desirability of isolating any particular stereoisomer. Thus, contrary to the Examiner's allegation, Jeffery does not expressly teach stereomerically pure isomers of compound 5a.

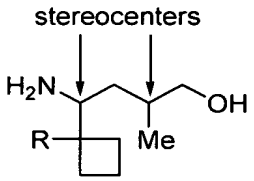
[3] The Examiner has pointed to compound 5a on page 2583, the last compound in column 1 on page 2587, and the last compound in column 1, on page 2588. (Office Action, page 2).



Jeffery silent as to confirguration of stereocenter.

compound 5a, Jeffery

With regard to the last compound in column 1, page 2587 (compound 4 in Jeffery), Applicants respectfully point out that Jeffery does not specify the stereoconfiguration of the compound's chiral centers, as shown below.

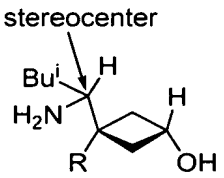


Configuration of stereocenters not specified in Jeffery; mixture of diastereomers isolated.

last compound in column 1, page 2587, Jeffery

Indeed, as stated in Jeffery, the compound is isolated "in the form of a 3.8:1 mixture of diastereoisomers." ((*See* Jeffery, page 2587, right column) (emphasis added)). Moreover, no attempts were made in Jeffery to separate and isolate the diastereomers, nor is there any suggestion regarding the desirability of performing such a separation. Thus, contrary to the Examiner's allegation, Jeffery does not expressly teach stereomerically pure isomers of the last compound in column 1, page 2587.

With regard to the last compound in column 1, page 2588 (compound 5b in Jeffery), Applicants respectfully point out that Jeffery is also completely silent as to the stereoconfiguration of the chiral center bearing the isobutyl moiety, as shown below.



Jeffery silent as to confirguration of stereocenter.

last compound in column 1, page 2588, Jeffery

Thus, contrary to the Examiner's allegation, Jeffery does not expressly teach stereomerically pure isomers of the last compound in column 1, page 2588.

In addition, Applicants respectfully submit that the Examiner does not point to any portion in Jeffery that would teach or suggest the desirability of any of the compounds referred to by the Examiner, much less the desirability of making any particular stereoisomer of such compounds.[4] In sum, Applicants respectfully point out that Jeffery does not disclose or suggest any of the compounds in their stereomerically pure form. Further, and perhaps more importantly, Jeffery does not suggest the desirability of any of the compounds referred to by the Examiner, much less the desirability of the stereoisomers of those compounds.

Housley does not cure the defect of Jeffery. While the Examiner has pointed to the compound disclosed in column 7, lines 48-49 in Housley ("the dimethyl derivative"), Claim 3 now recites a stereomerically pure isomer when R_1 and R_2 are both methyl. In this regard, Applicants respectfully submit that Housley does not disclose or suggest any specific stereoisomer of the dimethyl derivative.

While the Examiner has alleged that Housley "is expressly teaching that diastereoisomers and multiple chiral centers are old," Applicants respectfully submit that the Examiner, in support of this allegation, relies solely on a portion in Housley that merely provides a general description of diastereomers. (Office Action, page 2). However, completely absent from this general description is any teaching or suggestion that would prompt one of ordinary skill in the art to synthesize or isolate any specific stereoisomer among the millions of possible compounds encompassed in formula I of Housley, much less a stereoisomer of the dimethyl derivative.[5] Moreover, completely absent is any motivation to specifically select the dimethyl derivative itself from the hundreds of compounds disclosed in columns 5-8.

This lack of motivation is important because, to arrive at the stereoisomer of the dimethyl derivative, one would first have to be motivated to specifically select the dimethyl derivative from the infinite number of possible compounds disclosed in formula I of Housley, or at the very least, from the several hundred examples disclosed in Housley. Next, one

[4] Indeed, Jeffery provides information that would discourage those skilled in the art from investigating any of the compounds referred to by the Examiner, as discussed in more detail in Section 2, below.

[5] In fact, by defining its genus using terms such as "optionally substituted hydrocarbon group," without any limits as to the number of carbon atoms on the substitution, Housley discloses a genus that would encompass an infinite number of species. (*See e.g.* Housley, column 1, lines 13-27).

would have to be specifically motivated to isolate the stereoisomers. However, as set out above, no suggestion is provided in Housely or Jeffery for either of the steps.

In this regard, Applicants respectfully invite the Examiner's attention to a decision from the Board of Patent Appeals and Interferences (*In re Holy*, 2004 WL 77-12 (B.P.A.I. 2004, attached herewith as Exhibit A). In *In re Holy*, the Board stated:

> [i]n order to make a prima facie case of obviousness based on structural similarity, in this case similarity between the claimed optical isomer and its racemate taught by the prior art, not only must the structural similarity exist, but the prior art must also provide reason or motivation to make the claimed compound.

((*Id.)* (emphasis added)).

Consequently, in *In re Holy*, the Board held that prior disclosure of a racemic compound, without providing "reason or motivation to make" a claimed stereoisomer of the same compound, is insufficient for establishing *prima facie* case of obviousness. (2004 WL 77012 (B.P.A.I. 2004)).

In the instant case, similar to *In re Holy*, the Examiner merely points to a reference that discloses the racemate of the dimethyl derivative. Similar to *In re Holy*, the Examiner has not pointed to any portion in Housley that would provide one of ordinary skill in the art the motivation to make the stereomerically pure isomers of the dimethyl derivative. Merely pointing to a portion that discusses the possibility of the existence of stereoisomers and diastereomers is not enough, as the portion is merely stating general knowledge that is already known to one of ordinary skill in the art. Instead, as *In re Holy* shows, Examiner must provide a teaching or suggestion that would motivate one of skill in the art to specifically select the claimed compounds. Since the Examiner has not provided such a teaching or suggestion, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

For at least the foregoing reasons above, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. Thus, Applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn for this reason alone.

2. Jeffery teaches away from the claimed invention.

Even assuming, *arguendo*, a *prima facie* case of obviousness were established by Jeffery and Housley, Applicants respectfully submit that any presumption of obviousness should be rebutted in view of the fact that Jeffery actively teaches away from the current invention.

As the Examiner is aware, "[a] prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the invention." (MPEP §2141, *citing W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) (emphasis in original)). "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from flowing the path set out in the reference..." (*In re Gurley*, 27 F.3d 551, 553, 31 U.S.P.Q.2d 1130 (Fed. Cir. 1994) (emphasis added)). Indeed, "[a] reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." ((*Id.*) (emphasis added)).

In this regard, Applicants respectfully point out that, when considered as a whole, Jeffery teaches away form the claimed invention. This is because Jeffery, by providing that the pharmacological activity of sibutramine is "mediated predominantly by" two demethylated amines of sibutramine (Compounds 2 and 3), which are not recited by the pending claims, would have discouraged those skilled in the art from obtaining and investigating the compounds referred to by the Examiner (*e.g.* compounds 4 and 5a), much less the claimed stereoisomers of such compounds. (*See* Jeffery, page 2583, left side column). Thus, Applicants respectfully submit that any alleged *prima facie* case of obviousness has been rebutted. For this additional reason, Applicants respectfully request that the rejection under 35 U.S.C. §103 be withdrawn.

2. Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and thus, request that the rejections be withdrawn.

No fee is believed due for the submission of this paper. However, if any fees are due for the submission of this paper or to avoid abandonment of this application, please charge them to Deposit Account No. 50-3013.

Respectfully submitted,

Date: December 6, 2007

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Exhibit A

2004 WL 77012 (Bd.Pat.App. & Interf.)

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)

EX PARTE ANTONIN HOLY, HANA DVORAKOVA, ERIK D. A. DE CLERCQ, JAN M. R. BALZARINI

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

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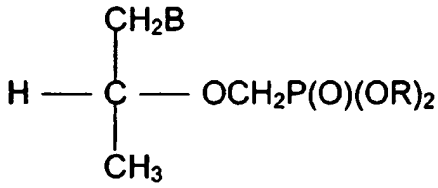
Before WINTERS, GRIMES, and GREEN
Administrative Patent Judges
GREEN
Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 4, 6, 8, 12-19, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94.[FN1] Claim 1 is representative of the subject matter on appeal, and reads as follows:

1. A compound of the formula:



(IA)

including salts of such compounds, wherein said compound of Formula IA is substantially free of its enantiomer and wherein B is (a) an unsubstituted purine moiety, (b) a substituted purine moiety substituted independently at the 2 and/or 6 and/or 8 position by amino, halogen, hydroxy, alkoxy, alkylamino, dialkylamino, aralkylamino, pyrrolidino, morpholino, piperidino, benzoylamino, azido, mercapto or alkylthio, or (c) the 8-aza analog thereof, and wherein

B is other than a guanine or 2-amino-6-halopurine;

R is H; and aryl in aralkylamino is a 6-10C aromatic group.

Claims 4, 6, 8, 70, 72, 73, 75, 85, 91, 93 and 94 further limit the compound of claim 1. Claims 12-19 are drawn to a method of preparing the compound of claim 1. Claims 45 through 48, 55, 63 and 65 are drawn to specific compounds that fall within the compound of claim 1.

The examiner relies upon the following references:

Hol [*sic*] et al. (Holy (US))	4,808,716	Feb. 28, 1989
Alexander et al. (Alexander)	5,130,427	Jul. 14, 1992
Yu et al. (Yu (US))	5,302,585	Apr. 12, 1994
Vemishetti et al. (Vemishetti)	5,476,938	Dec. 19, 1995
Webb, II et al. (Webb (US))	5,650,510	Jul. 22, 1997
European Patent Applications		
Holy et al. (Holy (EP))	0 253 412	Jul. 18, 1986
Webb, II (Webb (EP))	0 269 847	Jun. 08, 1988
Yu et al. (Yu (EP))	0 452 935	Oct. 23, 1991
Starrett et al. (Starrett)	0 481 214	Apr. 22, 1992

*2 Karrer, Organic Chemistry, 2nd English Edition, pp. 92-102 (1946)

The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 11th Edition, Article No. 7868, p. 1247 (1989)

In addition, appellants rely upon the following references:

DeClercq et al. (DeClercq), "Antiviral activity of phosphonylmethoxyalkyl derivatives of purine and pyrimidines," Antiviral Research, Vol. 8, pp. 261-272 (1987)

Holy et al. (Holy (1989)), "Phosphonylmethyl Ethers of Nucleosides and Their Acyclic Analogues," ACS Symposium Series, Vol. 401, pp. 51-71 (1989)

Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Webb (EP or US), Yu (US or EP), Starrett, Holy (EP) and Karrer. Claims 12-19 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Holy (EP), Webb (EP or US), Vemishetti, Alexander, Yu (US or EP) and the Merck Index. Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under the judicially created doctrine of obviousness-type double patenting over the claims of Holy (US), U.S. Patent No. 4,808,716 (the F716 patent) as combined with Yu (EP or US), Holy (EP), Starrett and Karrer. Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 72, 73, 75, 85, 91, 93 and 94 stand rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 5,650,510 (the 510 patent) as combined with Yu (EP or US), Holy (EP), Starrett and Karrer. Finally, claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of copending Application No. 07/925,610. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record except the provisional obviousness-type double-patenting rejection of claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 over copending Application No. 07/925,610.

DISCUSSION

Claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer. In addition, the obviousness-type double patenting rejections over the 716 patent and the 510 patent as combined with Yu (EP or US), Holy (EP), Starrett and Karrer are included in the analysis of the rejection over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer as the rejections state that the claims of the patents are "obvious variant[s] of that claimed herein as discussed in the above 103 rejection." Examiner's Answer, page 7. In addition, appellants rely on the patentability of the end product to overcome the rejection of claims 12-19 over the combination of Holy (US), Holy (EP), Webb (EP or US), Vemishetti (US), Alexander (US), Yu (US or EP) and the Merck Index. Thus, that rejection is also encompassed by the following analysis.

*3 Holy (US) is cited by the rejection for teaching a racemic mixture of 2-phosphonomethoxypropyladenine (PMPA). PMPA is included in the range of structures of claim 1. The rejection also references compound 2 in Table 1, as well as a discussion of the applications of the disclosed compounds, such as anti-viral activity, in column 4, lines 14-19 of the Holy (US) patent. The rejection reasons that:

> While the corresponding optical isomer is not particularly disclosed, the claimed R-isomer is held as an obvious variant in view of its very close structural similarity and the fact that one skilled in the art would recognize the existence of such isomers and expect one of a pair to perform better over the other. There is case law regarding the standards of patentability of optical isomers over the corresponding racemic mixture which is on point. See for example, In re Adamson, 125 USPQ 233; Eli Lilly vs. Generix, 174 USPQ 65 regarding the standards of patentability of optical isomers over the corresponding racemic mixture. Note Karrer, cited in

> Adamson, and applied herein is evidence that it is very well known considerably prior to applicants' effective filing to consider the separation of biologically active racemates in order to determine if one is largely responsible for the desired activity.

Examiner's Answer, page 5.

Webb (EP or US) is apparently cited for teaching derivatives of the compounds as taught by Holy (US). According to the rejection, "Webb does not embrace adenine compound of US Holy but does embrace substituted derivatives thereof having the same sidechain." Examiner's Answer, page 5. Yu (EP or US) is cited for its disclosure of resolution of one of the racemates disclosed by Webb "for elucidation of its antiviral properties," and teaches that the R isomer is "especially effective for treating HIV." Id. at 6.

Holy (EP) was cited for teaching compounds similar to the claimed compounds substituted with different groups, which also have anti-viral activity. Starrett was similarly cited for teaching "that for analogous phosphonate derivatives as claimed herein, substitution with alkyl- on the purine ring system at various ring positions is not a new modification." Id. at 6.

The examiner concludes:

> Thus it would have been obvious to one skilled in the art at the time the instant invention was made to expect instant optical isomers in main claim 1 and claims dependent thereon as well as various 2- and/or 6-substituted purines in independent claims 45-48, 55, 63 to be useful against one or more viruses in view of the close structural similarity and equivalency teachings outlined above.

Id.

***4** The panel would like to initially note that review of the issues on appeal was severely hampered by the lack of claim by claim analysis, i.e., the use of a shot-gun rejection. In rejecting claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 over the combination of Holy (US), Webb (EP or US), Yu, Starrett and Karrer, the examiner apparently cites Holy (EP) and Starrett for their teaching of certain derivatives that are only required in the dependent claims. Moreover, the rejection implies that at a minimum, claim 1 is would have been obvious over Holy alone.

Most tellingly, in the response to appellants' argument that Webb cannot be combined with Holy, the examiner responds that

> Webb is not a secondary reference but rather a primary reference applied for showing additional aspects of appellants' invention as obvious, mainly for its teaching of 2,6 diamino phosphonomethoxypropyl purine, but Webb also teaches and claims bases such as 2-amino purine, 8-substituted guanines (guanine per se is excluded in the instant claims) which are within at least claim 1.

Examiner's Answer, page 9.

If Webb was not to be combined with Holy (US), it should have been separately applied, or at least the examiner should have explicitly stated that Webb was being applied in the alternative. The way in which the rejection was laid out, however, makes it difficult to understand, much less rebut and review.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). In order to make a prima facie case of obviousness based on the structural similarity, in this case similarity between the claimed optical isomer and its racemate taught by the prior art, not only must the structural similarity exist, but the prior art must also provide reason or motivation to make the claimed compound. See In re Dillon, 919 F. 2d 688, 692,16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), In re Mayne, 104 F. 3d 1339, 1341, 41 USPQ2d 1451, 1454 (Fed. Cir. 1997); In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 256 (CCPA 1979). Moreover, the prior art has to enable the ordinary artisan to make the claimed compound. See Payne, 606 F.2d at 314. The rejection over Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer does not meet this criteria and thus fails to set forth a prima facie of obviousness.

In the rejection above, the examiner states with respect to the separation of the racemates of Holy (US) that "it is very well known considerably prior to applicants' effective filing to consider the separation of biologically active racemates in order to determine if one is largely

responsible for the desired activity," see Examiner's Answer, page 5, but does not set forth any facts or findings to support the motivational statement, especially since all that is currently being claimed is a single isomer, i.e., the R isomer. See In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1433-34 (Fed. Cir. 2002) (in reviewing an obviousness rejection, the court noted that "conclusory statements" as to teaching, suggestion or motivation to arrive at the claimed invention "do not adequately address the issue").

***5** With respect to the additional references cited by the examiner for teaching the various other substituents required by the claims, the only motivation that the examiner provides for making the combination is structural similarity. As noted above, however, structural similarity is not enough, but there must also be some teaching, suggestion, or motivation provided in the prior art to make the combination.

Moreover, appellants also argue that the art teaches away from isolating PMPA or PMPDAP from its isomer. Appellants cite Holy (1989) and DeClercq for teaching that PMPA is an inactive product. See Appeal Brief, pages 19-23. The examiner did not find the teaching away references to be persuasive because Holy filed and obtained a patent for PMPA and other compounds on the basis that the compounds are antiviral.

Obviousness is determined in view of the sum of all of the relevant teachings in the art, not isolated teachings in the art. See In re Kuderna, 426 F.2d 385, 389, 165 USPQ 575, 578 (CCPA 1970); see also In re Shuman, 361 F.2d 1008, 1012, 150 USPQ 54, 57 (CCPA 1966). In assessing the teachings of the prior art references, the examiner should also consider those disclosures that may teach away from the invention. See In re Geisler, 116 F.3d 1465, 1469, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997).

DeClercq states that PMPA is an "inactive product[]". DeClercq, page 264. The examiner dismisses that teaching by arguing that, in context, it appears that DeClercq is referring to the S-isomer. See Examiner's Answer, page 7. When a particular isomer is being referred to by the reference, however, DeClercq seems to indicate as such. Holy (1989) indicates that the replacement of the primary hydroxy group in HPMPA by a methyl group resulted in the loss of activity. See Holy (1989), pages 56-57. Thus, both DeClercq and Holy (1989) teach away from resolving a racemic mixture of PMPA into the currently claimed enantiomer.

In finding that the above prior art references do not teach away from separating a racemic mixture of PMPA into its optically pure isomers, the examiner relies on the Holy (US) patent, apparently bothered by the fact that Holy, who is also an inventor on the instant application, obtained a patent whose claims encompass PMPA. The examiner additionally asserts in support of the rejection that the patent was obtained because the compounds were shown to have antiviral activity.

While PMPA may be encompassed by the group of structures claimed in the Holy (US) patent, that is not dispositive of the issue of whether PMPA has antiviral activity. A claim may encompass inoperative embodiments and still meet the enablement requirement of 35 U.S.C. § 112, first paragraph. See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984), In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976).

***6** In Table 1 of the Holy (US) patent, specifically referred to by the examiner in rejecting the claims at issue, see Examiner's Answer, page 4, certain chemical characteristics are given for compound 2, i.e., PMPA, but the table does not set forth any biological data. The disclosure of Holy relied upon by the examiner as stating that PMPA has biological activity, i.e., column 4, lines 14-19 of the Holy (US) patent, also does not support the examiner's position. That portion of the patent states:

> Some compounds of the general formula I which are the subject of this invention, are important active components of antiviral drugs. An example of such compound is 9-phosphonylmethoxyethyladenine which exhibits a specific activity against DNA-viruses and Maloney sarcoma (PV 3018-85).

(Emphasis added). Thus, the patent does not assert that all of the compounds have antiviral activity, but that some of the compounds may have antiviral activity. When the disclosure of Holy (US) is read in conjunction

with the teachings of DeClercq and Holy (1989), which specifically address PMPA, teaching that compounds such as PMPA do not have antiviral activity, the prior art, when read as a whole, teaches away from separating a racemic mixture of PMPA into its optically pure isomers.

In addition, the examiner also relies upon Adamson and Eli Lilly as apparently standing for the proposition that an optically pure form of a compound is per se obvious over a disclosure of a racemic mixture of the compound. See Examiner's Answer, page 8 ("The motivation to resolve the racemate of Holy is fully supported by the case law previously cited dealing with racemates vs. individual optical isomers."). One cannot rely on case law alone, however, to provide the motivation to modify a prior art compound. "[T]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." In re Rouffet, 149 F.3d 1350, 1356, 47 USPQ2d 1453, 1456 (Fed. Cir. 1998) (citations omitted). In this case, the prior art as a whole, as discussed above, teaches away from making the modification as suggested by the examiner.

Claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 stand provisionally rejected over the claims of co-pending Application No. 07/925,610. As appellants do not present any arguments as to why the rejection is improper, but instead note their intent to file a terminal disclaimer once the copending case is sent to issue, this rejection is affirmed.

CONCLUSION

The rejection of claims 1, 4, 6, 8, 45-48, 55, 63, 65, 70, 72, 73, 75, 85, 91, 93 and 94 over the combination of Holy (US), Webb (EP or US), Yu (EP or US), Starrett, Holy (EP) and Karrer is reversed. For the same reasons, the obviousness-type double patenting rejections over the 716 patent and the 510 patent as combined with Yu (EP or US), Holy (EP), Starrett and Karrer, and the rejection of claims 12-19 over the combination of Holy (EP), Webb (EP or US), Vemishetti, Alexander, Yu (US or EP) and the Merck Index, are also reversed. Finally, the provisional rejection of claims 1, 4, 6, 70, 72, 85, 91, 93 and 94 over the claims of co-pending application No. 07/925,610 is affirmed.

*7 No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART; REVERSED-IN-PART

BOARD OF PATENT APPEALS AND INTERFERENCES

SHERMAN D. WINTERS

Administrative Patent Judge

ERIC GRIMES

Administrative Patent Judge

LORA M. GREEN

Administrative Patent Judge

FN1. According to the Examiner's Answer, claims 49-54, 56-62, 64 and 79 are free of the prior art, with Claim 79 being objected to, and thus these claims are not subject to the instant appeal. See Examiner's Answer, page 2.

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